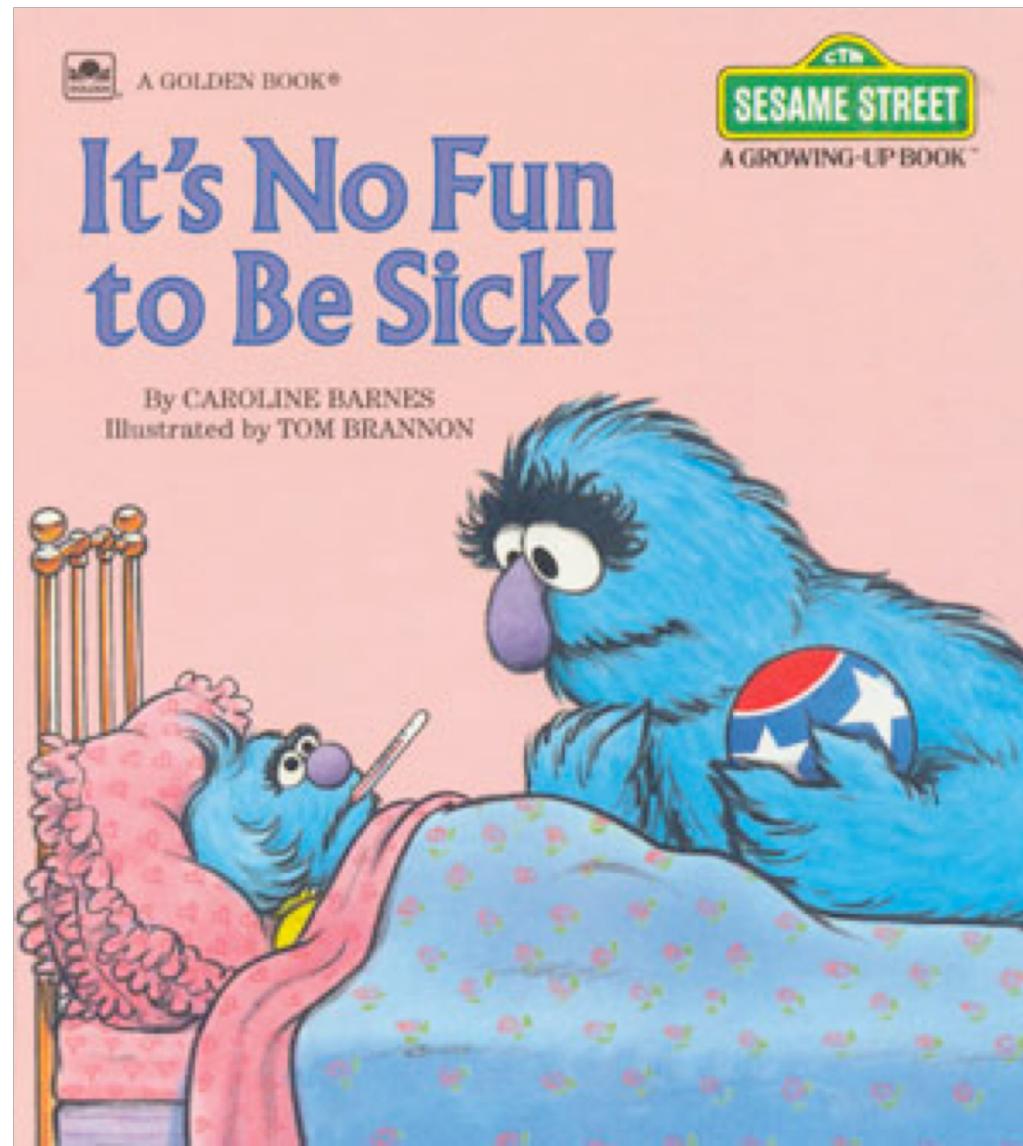
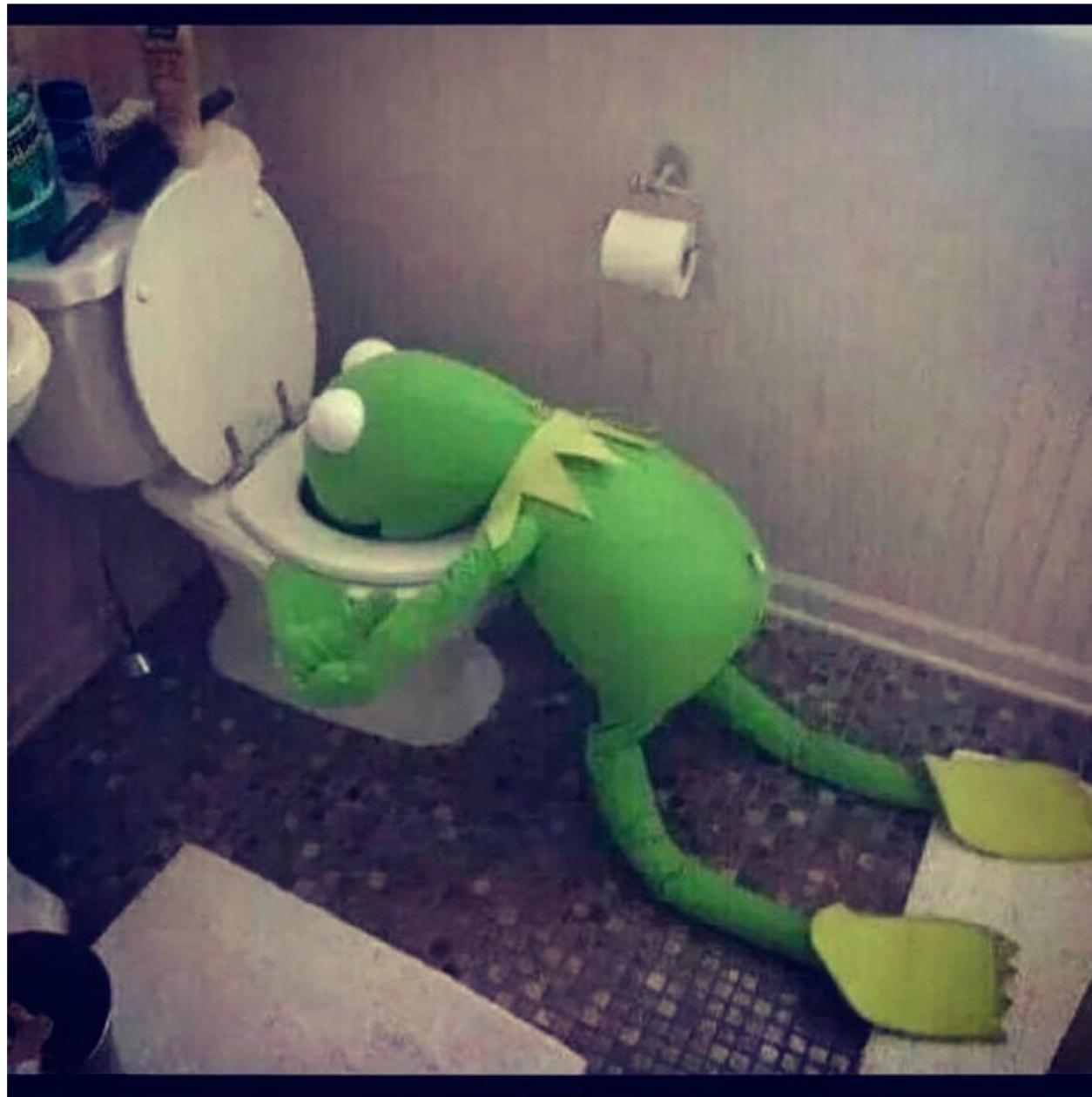


HOST POPULATION GENOMIC APPLICATIONS IN DISEASE



HOST POPULATION GENOMIC APPLICATIONS IN DISEASE



OUTLINE

(ME TALKING: ~20 MINS)

- I. MOLECULAR APPROACHES FOR POPULATION GENOMICS
- II. HOST LANDSCAPE GENOMIC APPROACHES
- III. HOST DISEASE RESISTANCE
- IV. HOST INBREEDING DEPRESSION-DISEASE INTERACTIONS

(YOU THINKING, US DISCUSSING: ~20 MINS)

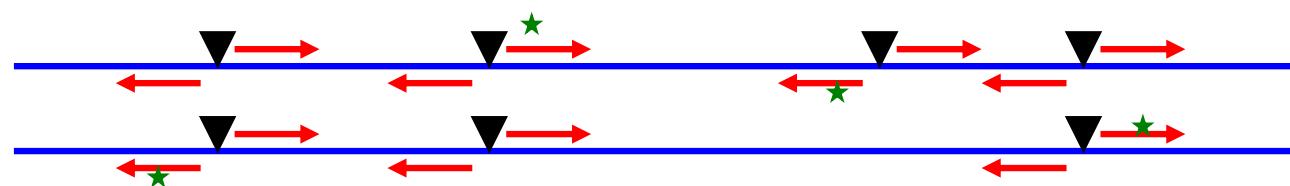
- V. PAIRS: “FLASH” HOST POP GENOMICS RESEARCH DESIGN
- VI. GROUP DISCUSSION OF RESEARCH IDEAS

POPULATION GENOMIC APPROACHES

| Method name | Brief description |
|--|--|
| Whole-genome sequencing (WGS; Pritchard 2011) | Sequencing of the entire genome, usually using shotgun sequencing. Can range from development of an annotated reference genome using high coverage to resequencing at low depth. |
| Restriction site-associated DNA sequencing (RAD-seq; Andrews <i>et al.</i> 2016) | A suite of reduced representation methods that sequence and genotype loci adjacent to restriction sites |
| Targeted capture (Jones & Good 2016) | A reduced representation method that enriches for targeted regions of the genome using labeled oligonucleotides |
| Ultraconserved elements (UCE; Faircloth <i>et al.</i> 2012) | Highly conserved regions of the genome that can be used to generate sequence data at orthologous loci from evolutionarily distant taxa |
| Anchored phylogenomics (Lemmon <i>et al.</i> 2012) | Sequencing and genotyping of libraries enriched for UCEs, anonymous, and/or functional loci |
| Transcriptomics (e.g., RNA-seq; Wang <i>et al.</i> 2009) | Analysis of gene expression levels, usually conducted by sequencing cDNA from RNA (RNA-seq) |

Genomic Tools

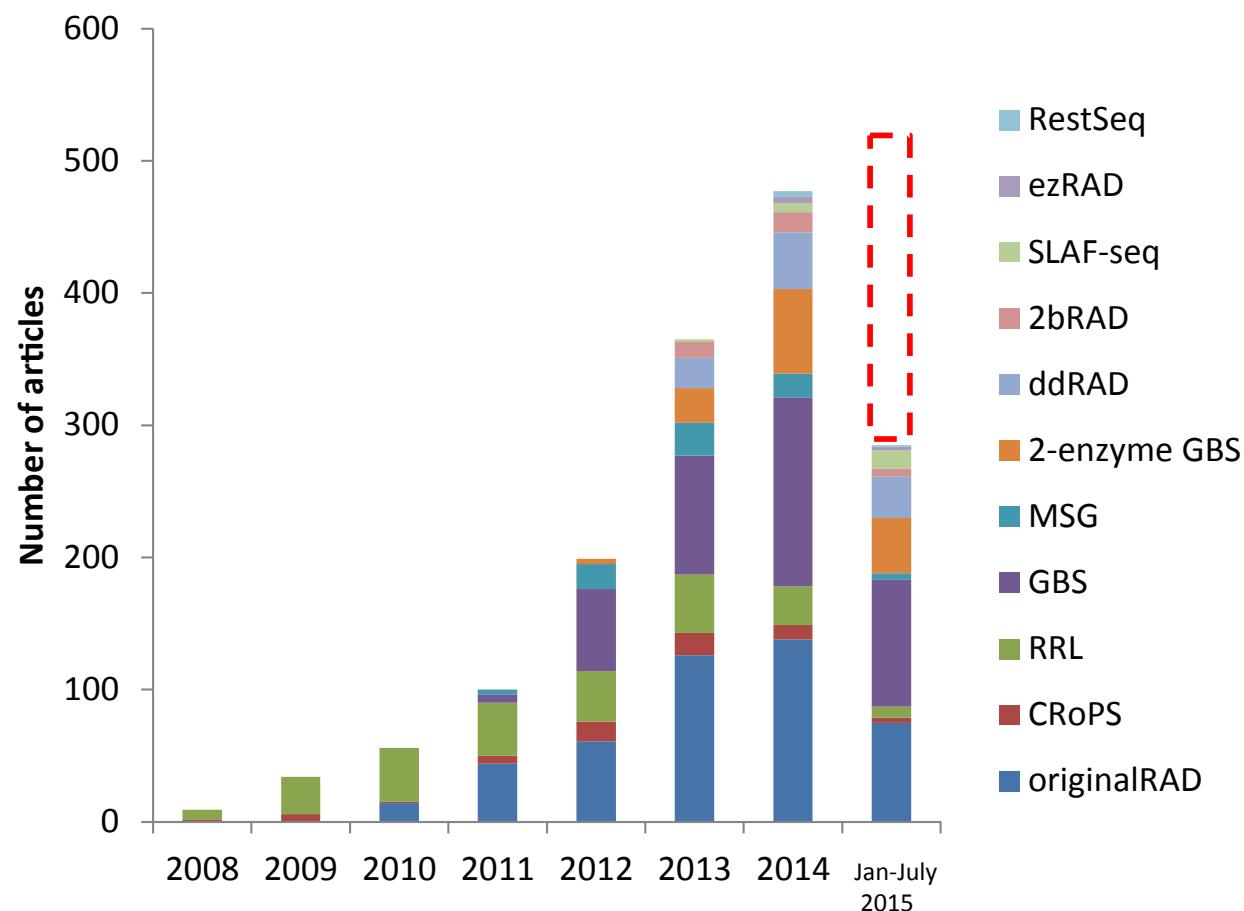
- Whole-genome resequencing
- Transcriptome sequencing
- Targeted sequencing
 - Exon capture
- Anonymous genomic sequencing
 - Restriction enzyme-based methods (RAD sequencing)



Davey et al (2011) *Nat Rev Genet* 12:499
Andrews et al (2016) *Nat Rev Genet* 17:81

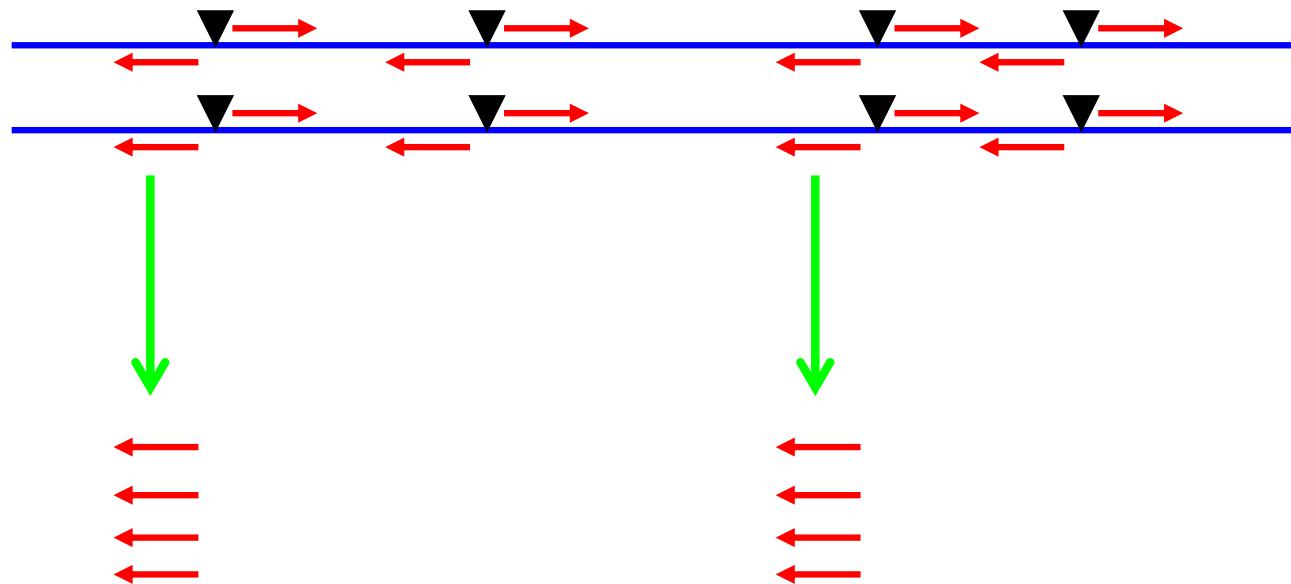
Harnessing the power of RADseq for ecological and evolutionary genomics

Kimberly R. Andrews¹, Jeffrey M. Good², Michael R. Miller³, Gordon Luikart⁴
and Paul A. Hohenlohe⁵

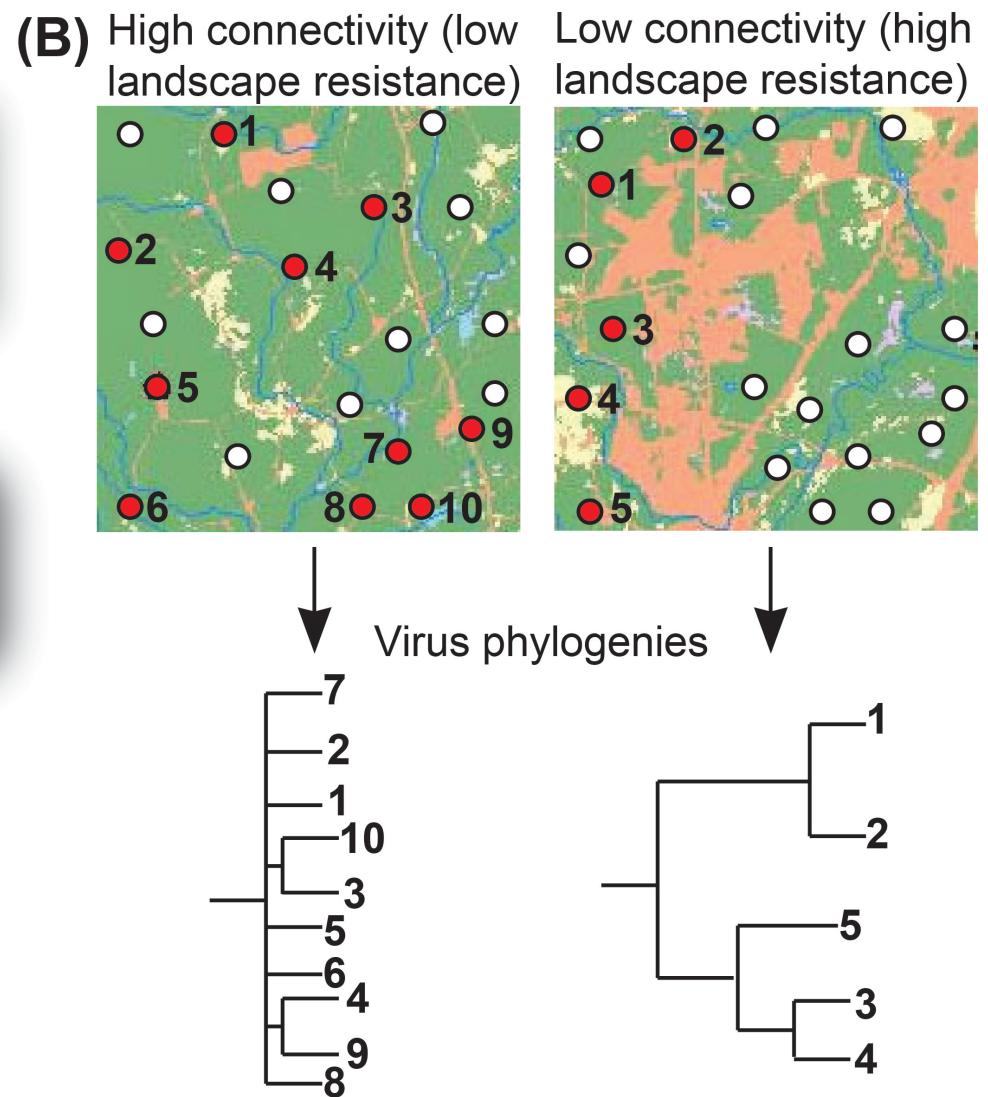
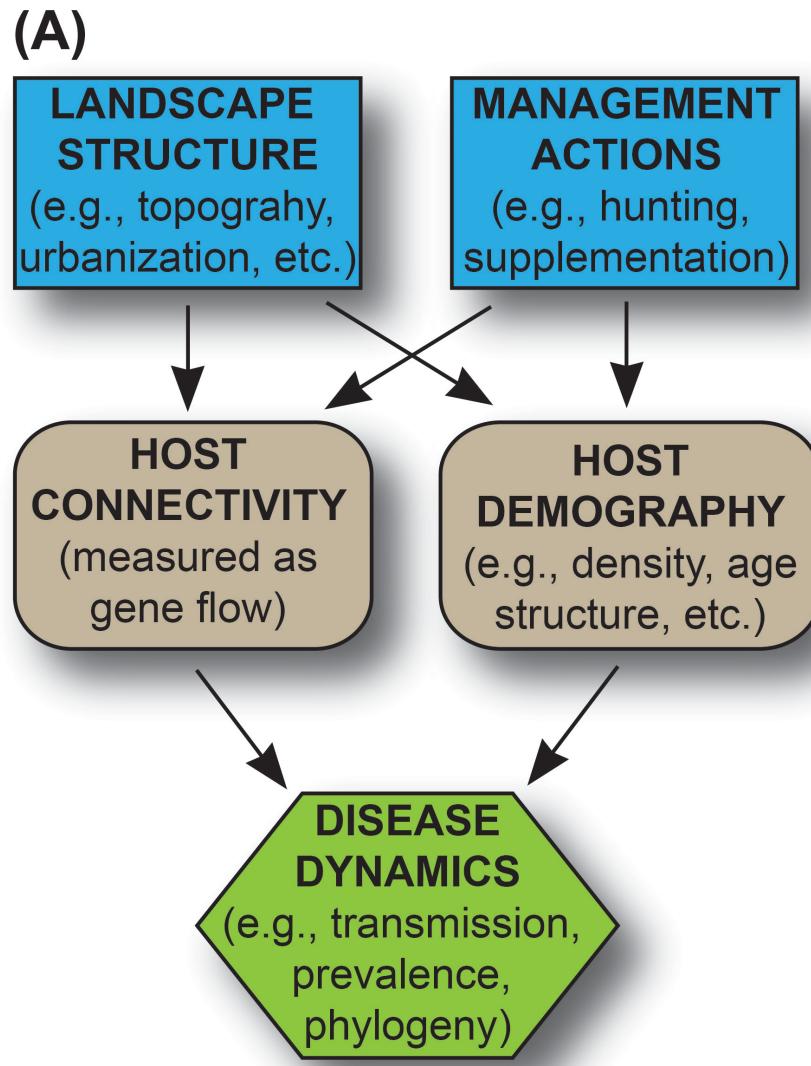


Genetics of disease phenotypes

- RAD + capture = Rapture (Ali et al 2016 Genetics 202:389)



LANDSCAPE GENOMICS: GENERAL IDEA



LANDSCAPE GENOMICS: HOST CONNECTIVITY EXAMPLE

MOLECULAR ECOLOGY

Molecular Ecology (2010) 19, 3515–3531

doi: 10.1111/j.1365-294X.2010.04679.x

The landscape genetics of infectious disease emergence and spread

ROMAN BIEK* and LESLIE A. REAL†‡

*Division of Ecology and Evolutionary Biology, Boyd Orr Centre for Population and Ecosystem Health, University of Glasgow, Glasgow G12 8QQ, UK, †Department of Biology, Center for Disease Ecology, Emory University, 1510 Clifton Road, Atlanta, GA 30322, USA, ‡Fogarty International Center, National Institutes of Health, Bethesda, MD 20892, USA

LANDSCAPE GENOMICS: HOST CONNECTIVITY EXAMPLE

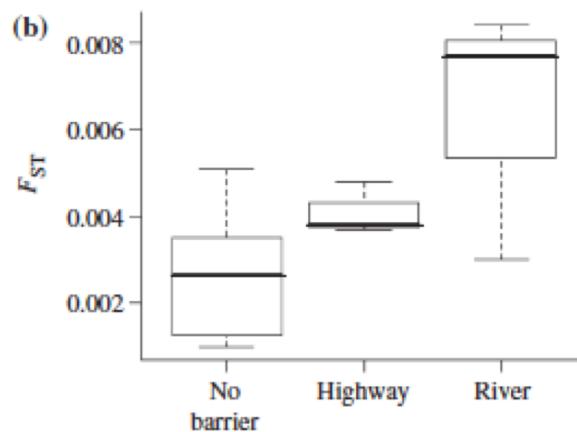
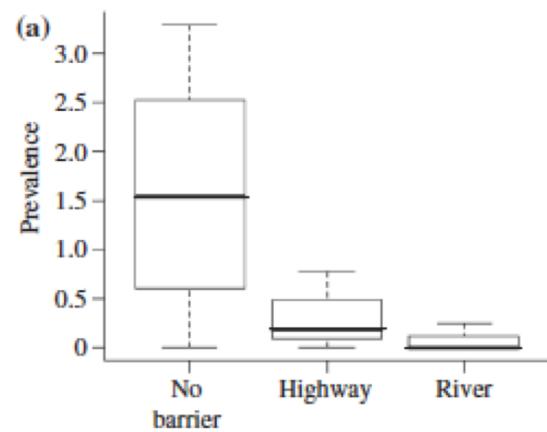


Fig. 1 Chronic wasting disease (CWD) in white-tailed deer as an example of using host population genetics to identify landscape determinants of disease spread. (a) Prevalence of CWD in 15 study areas in Wisconsin and (b) genetic differentiation (F_{ST}) of deer host populations in study areas relative to core area of CWD infection, with study areas grouped based on the type of landscape feature separating them from the core area. Reprinted from Blanchong *et al.* (2008) with permission.

LANDSCAPE GENOMICS: DIVERGENT SELECTION EXAMPLE

MOLECULAR ECOLOGY

Molecular Ecology (2016) 25, 324–341

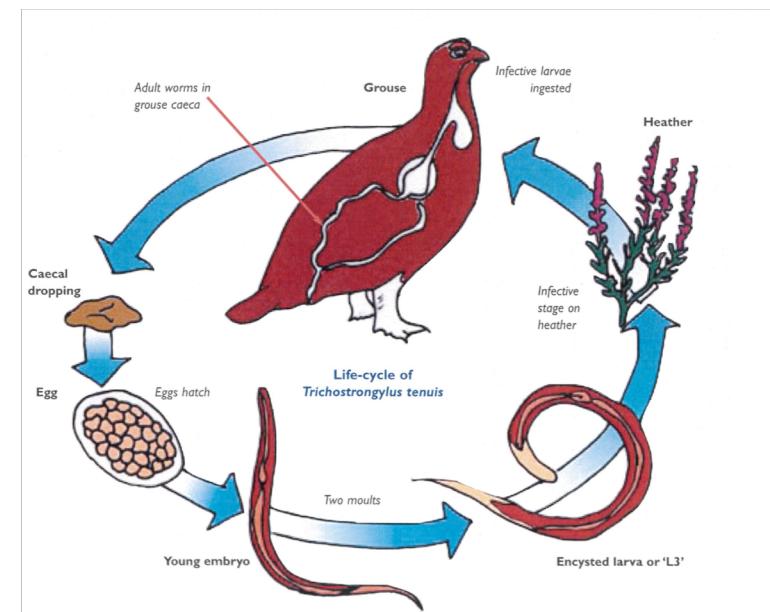
doi: 10.1111/mec.13473

DETECTING SELECTION IN NATURAL POPULATIONS: MAKING SENSE OF GENOME SCANS AND TOWARDS ALTERNATIVE SOLUTIONS

The role of parasite-driven selection in shaping landscape genomic structure in red grouse (*Lagopus lagopus scotica*)

MARIUS A. WENZEL, ALEX DOUGLAS, MARIANNE C. JAMES,¹ STEVE M. REDPATH and STUART B. PIERTNEY

Institute of Biological and Environmental Sciences, University of Aberdeen, Tillydrone Avenue, Aberdeen AB24 2TZ, UK



LANDSCAPE GENOMICS: DIVERGENT SELECTION EXAMPLE

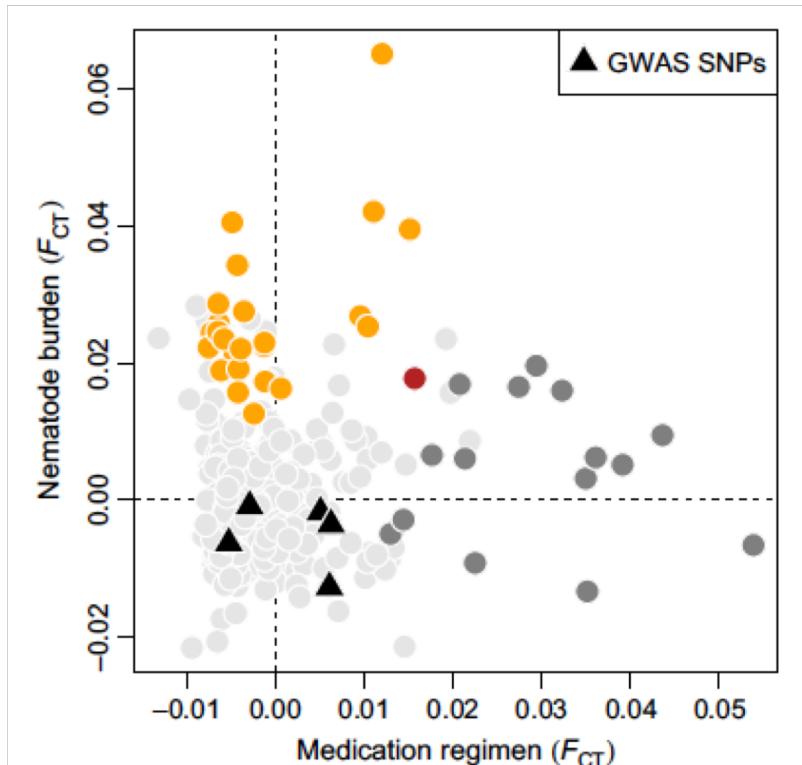
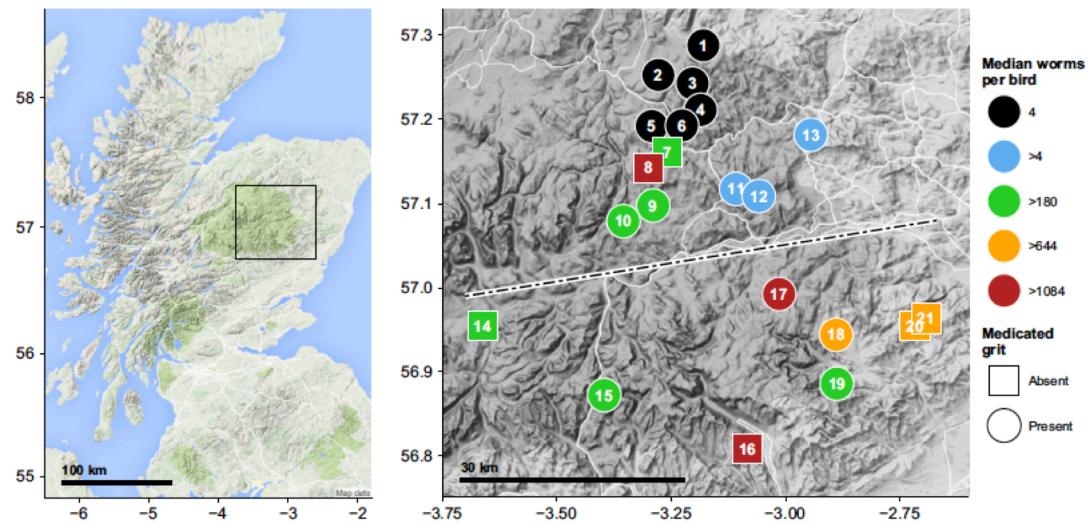


Fig. 2 Graphical summary of SNP-by-SNP hierarchical AMOVA testing for genetic differentiation among populations grouped by median nematode burden or anthelmintic medication regimen. Each data point represents the degree of genetic differentiation among population groups (F_{CT}) at a single SNP. Statistically significant F_{CT} estimates (single-test $P \leq 0.05$) are colour-coded (dark grey: medication regimen; orange: nematode burden; red: both; all SNPs not significant with FDR-corrected $q > 0.1$). Five candidate SNPs for nematode-driven selection previously highlighted by genome-wide association (GWAS SNPs) are displayed as black triangles.

DISEASE RESISTANCE: GENERAL IDEA

THREE GENERAL APPROACHES:

1. CANDIDATE GENES
2. GENOME-WIDE ASSOCIATION STUDIES
3. TRANSCRIPTOMICS

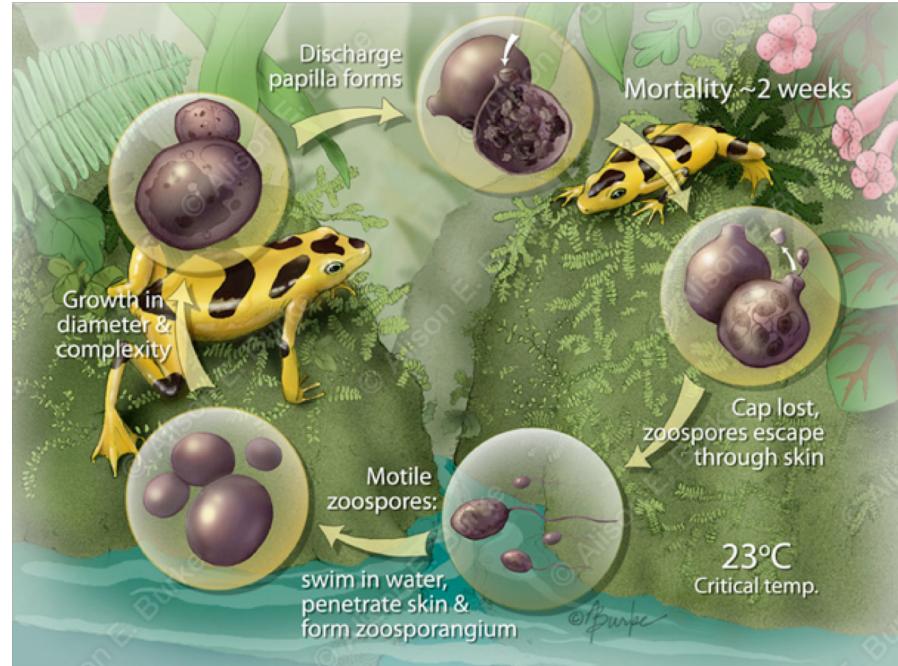
DISEASE RESISTANCE: CANDIDATE GENE EXAMPLE



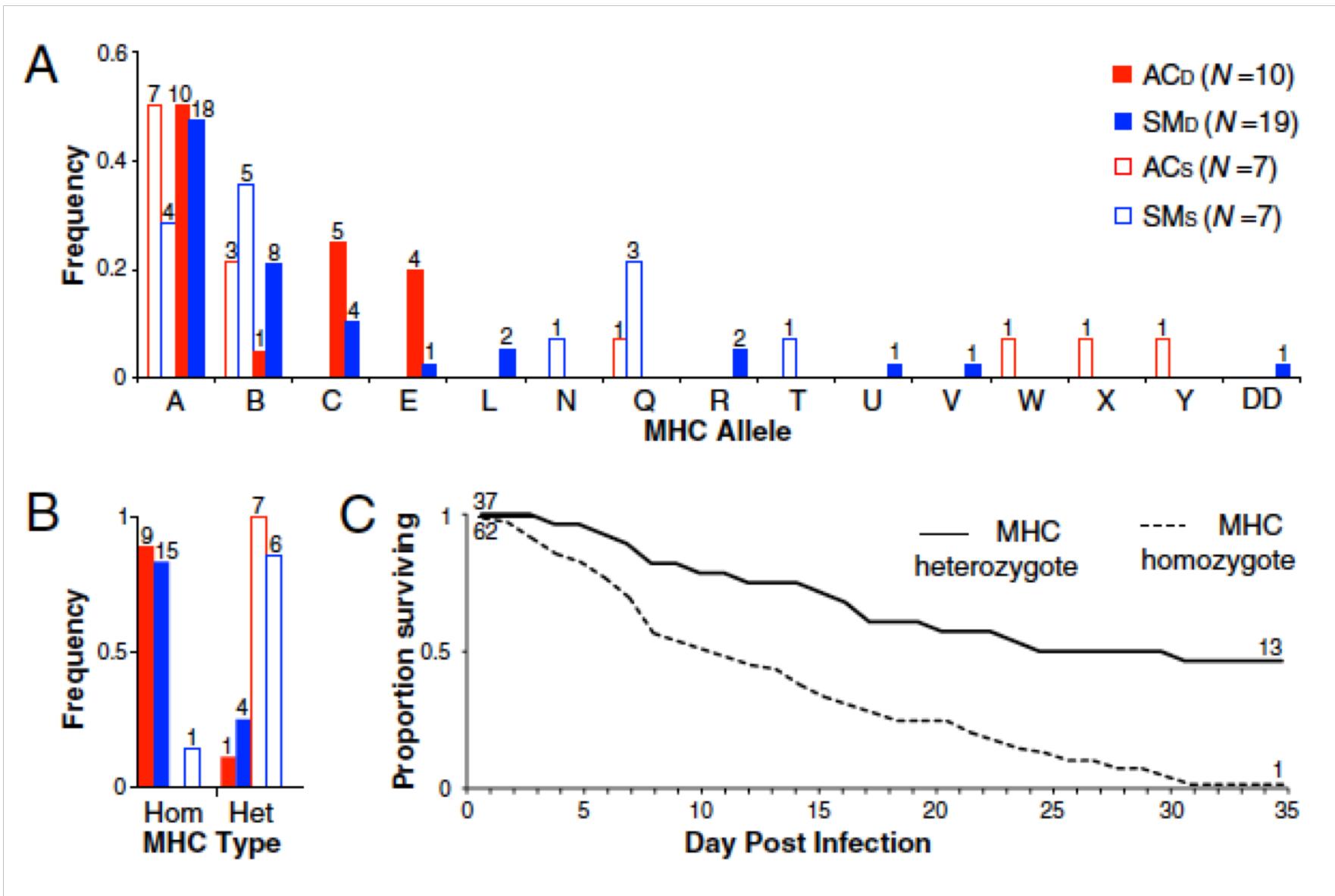
MHC genotypes associate with resistance to a frog-killing fungus

Anna E. Savage¹ and Kelly R. Zamudio

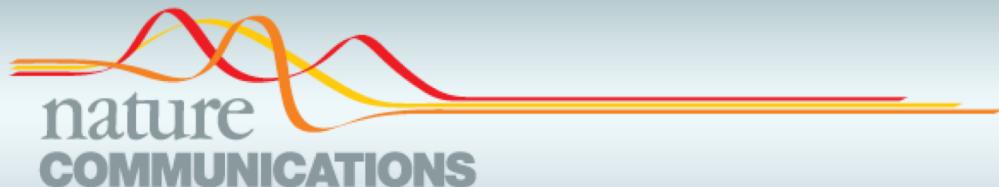
Department of Ecology and Evolutionary Biology, Cornell University, Ithaca, NY 14853



DISEASE RESISTANCE: CANDIDATE GENE EXAMPLE



DISEASE RESISTANCE: GWAS EXAMPLE



ARTICLE

Received 31 Mar 2016 | Accepted 20 Jul 2016 | Published 30 Aug 2016

DOI: 10.1038/ncomms12684

OPEN

Rapid evolutionary response to a transmissible cancer in Tasmanian devils

Brendan Epstein¹, Menna Jones², Rodrigo Hamede², Sarah Hendricks³, Hamish McCallum⁴, Elizabeth P. Murchison⁵, Barbara Schönfeld², Cody Wiench³, Paul Hohenlohe^{3,*} & Andrew Storfer^{1,*}



DISEASE RESISTANCE: GWAS EXAMPLE



ARTICLE

Received 31 Mar 2016 | Accepted 20 Jul 2016 | Published 30 Aug 2016

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DISEASE RESISTANCE: TRANSCRIPTOMICS EXAMPLE

MOLECULAR ECOLOGY

Molecular Ecology (2016) 25, 5663–5679

doi: 10.1111/mec.13871

Comparative study of host response to chytridiomycosis in a susceptible and a resistant toad species

T. J. POORTEN and E. B. ROSENBLUM

Department of Environmental Science, Policy and Management, University of California, Rm. 54 Mulford Hall, Berkeley, CA, USA



DISEASE RESISTANCE: TRANSCRIPTOMICS EXAMPLE

Table 1 Summary of gene expression results from GO stats enrichment analysis

| Group | | No. of DE probesets* | No. of enriched GO Terms [†] | Selected enriched GO Terms |
|-----------------------|------|----------------------|---------------------------------------|---|
| Skin: Upregulated | | | | |
| <i>Bufo marinus</i> | 487 | 66 | | Epidermis development; wound healing; cell proliferation; apoptotic signalling pathway; response to stress; metabolic process; biological adhesion; immune system development |
| <i>Bufo boreas</i> | 1108 | 68 | | Regulation of complement activation; response to stress; wound healing; cell redox homeostasis; response to external stimulus; response to yeast; haematopoietic or lymphoid organ development; leucocyte migration; apoptotic process; cellular metabolic process; innate immune response; coagulation |
| Skin: Downregulated | | | | |
| <i>B. marinus</i> | 70 | 2 | | Cellular localization; metabolic process |
| <i>B. boreas</i> | 1055 | 58 | | Collagen catabolic process; extracellular structure organization; blood vessel development; response to wounding; haemostasis; cell-matrix adhesion; tissue development; epithelium development; actin cytoskeleton organization |
| Liver: Upregulated | | | | |
| <i>B. marinus</i> | 0 | NA | | — |
| <i>B. boreas</i> | 1947 | 70 | | Vesicle-mediated transport; protein folding; regulation of cell cycle; cellular metabolic process; RNA processing; cellular respiration; cell proliferation; response to stress |
| Liver: Downregulated | | | | |
| <i>B. marinus</i> | 2 | NA | | — |
| <i>B. boreas</i> | 951 | 74 | | Actin filament organization; wound healing; response to stress; immune system process; complement activation; antigen processing and presentation of peptide antigen; innate immune response; blood coagulation; blood vessel morphogenesis |
| Spleen: Upregulated | | | | |
| <i>B. marinus</i> | 0 | NA | | — |
| <i>B. boreas</i> | 0 | NA | | — |
| Spleen: Downregulated | | | | |
| <i>B. marinus</i> | 0 | NA | | — |
| <i>B. boreas</i> | 3 | NA | | — |

*Differential expression (DE) threshold criteria for *B. marinus* was BH-corrected *P*-value < 0.1; and for *B. boreas* was BH-corrected *P*-value < 0.05.

[†]List of 'Biological Process' category GO terms was reduced using Revigo to remove semantic redundancies.

DISEASE RESISTANCE: INBREEDING DEPRESSION-DISEASE INTERACTION EXAMPLE

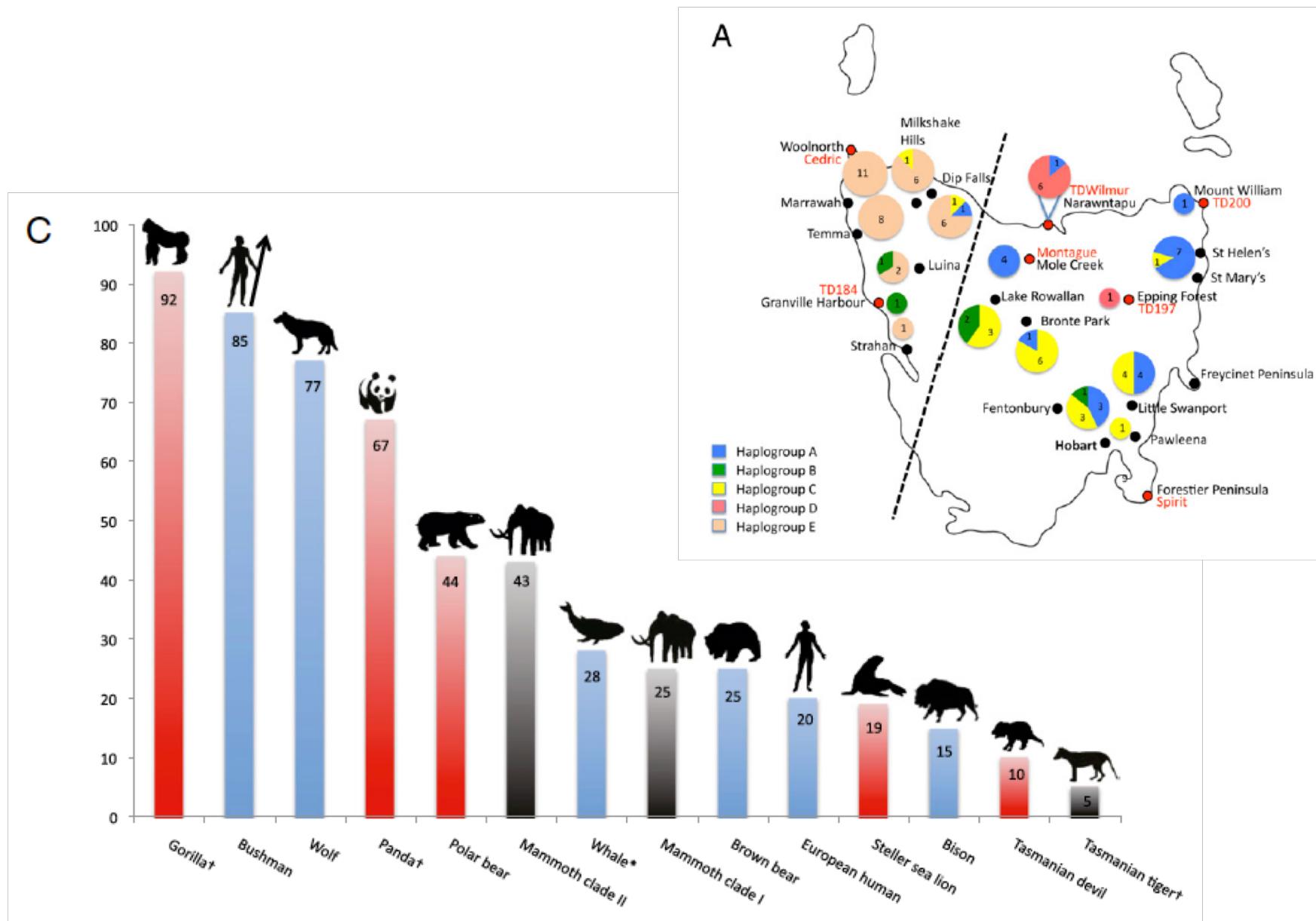
PNAS

Genetic diversity and population structure of the endangered marsupial *Sarcophilus harrisii* (Tasmanian devil)

Webb Miller^{a,1}, Vanessa M. Hayes^{b,c,1,2}, Aakrosh Ratan^a, Desiree C. Petersen^{b,c}, Nicola E. Wittekindt^a, Jason Miller^c, Brian Walenz^c, James Knight^d, Ji Qi^a, Fangqing Zhao^a, Qingyu Wang^a, Oscar C. Bedoya-Reina^a, Neerja Katiyar^a, Lynn P. Tomsho^a, Lindsay McClellan Kasson^a, Rae-Anne Hardie^b, Paula Woodbridge^b, Elizabeth A. Tindall^b, Mads Frost Bertelsen^e, Dale Dixon^f, Stephen Pyecroft^g, Kristofer M. Helgen^h, Arthur M. Lesk^a, Thomas H. Pringleⁱ, Nick Patterson^j, Yu Zhang^a, Alexandre Kreiss^k, Gregory M. Woods^{k,l}, Menna E. Jones^k, and Stephan C. Schuster^{a,1,2}



DISEASE RESISTANCE: INBREEDING DEPRESSION-DISEASE INTERACTION EXAMPLE



PAIRS: “FLASH” HOST POP GENOMICS RESEARCH DESIGN

INSTRUCTIONS:

1. COME UP WITH QUESTION & HYPOTHESIS FOR YOUR HOST SPECIES RELATED TO DISEASE
1. DISCUSS WHICH GENOMIC APPROACHE(S) WOULD BEST TEST YOUR HYPOTHESIS
2. IN ~10 MINS, WILL DISCUSS RESEARCH IDEAS WITH GROUP

